REMARKS

Claim Amendments

Claims 34-37, 49 and 52 have been canceled herein. Claims 45-48 have been amended herein to recite that the agent is a histone deacetylase small molecule inhibitor and new Claims 53-54 have been added herein. Support for the claim amendments and new claims can be found throughout the specification and in Claims 47-50 as originally filed. No new matter has been added.

Rule 1.48(a) Petition

According to the Office Action, the petition under Rule 1.48(a) to correct the inventorship in the instant application is not present within the file. Applicants enclose herewith a copy of the date-stamped postcard receipts and documents filed with the USPTO in support of the petition. Entry of the petition and the correction of inventorship in the instant application is respectfully request.

Claim Objections

Claim 45 is objected to do to the presence of specific informalities. Claim 45 has been amended herein to correct the informalities. Reconsideration and withdrawal of the objection are respectfully requested.

Double Patenting

Claims 34-36 and 45-49 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claim 20 of copending U.S. Application No. 09/563,728.

Claims 34-36 have been canceled herein, thus rendering the rejection as it applies to these claims moot. Claims 45-48 have been amended herein to recite that the agent is a histone deacetylase small molecule inhibitor, which is not encompassed within the scope of Claim 20 of copending U.S. Application No. 09/563,728. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 34 and 45-52 Under 35 U.S.C. §112, First Paragraph

Claims 34 and 45-52 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Claims 34, 49 and 51-52 have been canceled herein, thus rendering the rejection as it applies to these claims moot. Applicants will address the rejection as it applies to the remaining claims.

The Office Action has alleged that the following elements of the invention are not adequately described by the specification: (1) the structure of histone deacetylase isoforms from all species; (2) representative structures of all types of inhibitor encompassed by the claims; and (3) how to identify an inhibitor as one that will inhibit more than one histone deacetylase isoforms but less than all histone deacetylase isoforms.

With respect to point (1), claims 45 and 50 have been amended to indicate that the histone deacetylase inhibitor is a small molecule inhibitor. This issue has been rendered moot.

With respect to point (2), as stated above, the present claims have been amended to indicate that the agent is a small molecule inhibitor. As the claims no longer encompass that the agent is an oligonucleotide, Applicant believes that the amendments render objections to such subject matter moot. Representative examples of small molecule inhibitors are presented in the specification (Table 2, page 7). As indicated in paragraph [0010], of the application as published, all of the previously known inhibitors of histone deacetylase are non-specific for a particular histone deacetylase isoforms, i.e., they are pan-inhibitors. As further indicated in paragraph [0013], the inventors have discovered new agents that inhibit specific HDAC isoforms.

With respect to point (3), examples 8-13 and Table 2 teach the structure of small molecule inhibitors that inhibit some isoforms but less than all isoforms and how they were synthesized. It is not possible for Applicants to list every possible small molecule that fits this description nor are they required to do so. However, the specification does provide examples that one skilled in the art would be able to use to determine whether or not a small molecule is an inhibitor of some isoforms but less than all isoforms. Specifically, paragraphs [0111] and [0153]-[0156] provide the skilled artisan with the ability to identify a particular small molecule inhibitor as one that will inhibit more than one specific histone deacetylase isoforms but less than all isoforms. Therefore, as Applicants provide examples of small molecules that inhibit some but less than all HDAC isoforms and teach how this characteristic is to be identified, the

specification satisfies the written description requirement. Reconsideration and withdrawal are respectfully requested.

Rejection of Claims 34-37, 45-49 and 52 Under 35 U.S.C. §112, First Paragraph

Claims 34-37, 45-49 and 52 are rejected under 35 U.S.C. §112, first paragraph, because, according to the Office Action, the specification, while being enabling for inhibition of histone deacetylase gene expression using nucleic acid modulators in cells *in vitro*, does not reasonably provide enablement for inhibition of histone deacetylase using antisense oligonucleotides *in vivo*. Claims 34-37, 49 and 52 have been canceled herein, and Claims 45-48 have been amended herein to recite that the agent is a histone deacetylase small molecule inhibitor, thus rendering the rejection as it applies to these claims moot. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of Claims 45-48 Under 35 U.S.C. §102(b)

Claims 45-48 are rejected under 35 U.S.C. §102(b) as anticipated by Jones et al. (Nature Genetics, 1998, of record). According to the Office Action, Jones et al. disclose contacting a cell with TSA, a small molecule inhibitor of histone deacetylase (HDAC). However, TSA is a pan-inhibitor (i.e., it is non-specific) and inhibits **all** HDAC isoforms.

Claims 45-48 have been amended herein to recite that the agent is a histone deacetylase small molecule inhibitor which inhibits one or more specific histone deacetylase isoforms but less that all (i.e., a non-pan-inhibitor), which is not anticipated by Jones et al. Therefore, Jones et al. fails to anticipate Claims 45-48. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 34 and 45-51 Under 35 U.S.C. §102(b)

Claims 34 and 45-51 are rejected under 35 U.S.C. §102(b) as being anticipated by Kwon et al. (Proc. Natl. Acad. Sci. USA 1998, vol. 95, pages 3356-3361). According to the Office Action, Kwon et al. disclose a small molecule inhibitor which inhibits histone deacetylase (HDAC) 1. Kwon et al. assayed the molecule depudecin in crude extracts and against recombinant HDAC-1 enzyme. No assays were performed on other specific HDAC enzymes.

Claims 34 and 49 have been canceled herein and Claims 45-48 have been amended herein to recite that the agent is a histone deacetylase small molecule inhibitor which inhibits one or more specific histone deacetylase isoforms but less that all, which is not anticipated by Kwon et al. Therefore, Kwon et al. fails to anticipate claims 45-51. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 34-36 and 45-49 Under 35 U.S.C. §102(e)

Claims 34-36 and 45-49 are rejected under 35 U.S.C. §102(e) as being anticipated by MacLeod et al. (US 2003/0078216).

Claims 34-36 and 49 have been cancelled herein, thus rendering the rejection as it applies to these claims moot. Claims 45-48 have been amended herein to recite that the agent is a histone deacetylase small molecule inhibitor, which is not encompassed within the teachings of MacLeod et al. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 45-48 Under 35 U.S.C. §103(a)

Claims 45-48 are rejected under 35 U.S.C. §103(a) as being unpatentable over Sambucetti et al. (Journal of Biological Chemistry 1999, vol. 274, pages 34940-34947), Taunton et al. (Science 1996, cited on IDS), Baracchini et al. (US 5,801,154) and Bennett et al. (US 5,998,148).

Claims 45-48 have been amended herein to recite that the agent is a histone deacetylase small molecule inhibitor which inhibits one or more specific histone deacetylase isoforms but less that all. The combination of the cited references fails to teach or suggest the claimed invention. Reconsideration and withdrawal of the rejection are respectfully requested.

Applicants also wish to note that the Office Action, on page 16, second paragraph, states that Sambucetti *et al.* teach that inhibition of histone deacetylase-1 can inhibit tumor cell proliferation. However, Sambucetti *et al.* teach that total histone deacetylase activity in whole cell extracts was completely inhibited by 1nM TPX (see first paragraph of Results section and Figure 1) and that TPX induces cell cycle arrest or apoptosis in human tumor cell lines *in vitro* (paragraph bridging pages 34942-34943); there is no teaching that inhibition of histone deacetylase-1 can inhibit tumor cell proliferation.

Conclusion

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

Dated: June 29, 2006

By: Joseph C Zucchero
Joseph C. Zucchero
Registration No. 55,762

Keown & Associates
500 West Cummings Park
Suite 1200
Woburn, MA 01801
Telephone: 781-938-1805
Facsimile: 781-938-4777